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CASE

OF

POISONING BY THREE GRAINS OF ATROPIA.

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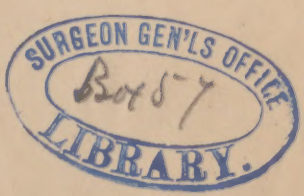

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CASE OF POISONING BY ATROPIA.

On the 3d of November, 1868, I was requested by Dr. De Young, of this city, to see his sister, Mrs. H., a stout, healthy woman, forty-three years of age, who was labouring under symptoms of narcotic poisoning. At 8.20 A. M. she had taken, her stomach being empty at the time, four pills compounded from a prescription which he had made some time previously, and of which the following is a true and literal copy :—

℞.—Hydrarg. chlor. mite, ext. rhei, āā ℈ss; asafœt. gr. iij; ft. pil. No. IV. 6. 22. 8.—P. De Young.

Mrs. H. had been in the habit of taking the above pills for the relief of constipation and headache, and had always obtained them from the same drug store. On the morning in question, about twenty minutes after having swallowed the dose, her maid heard herself called twice by some one with a strange, husky voice, and, upon entering the room, found, to her surprise, that she had been called by Mrs. H., who was dropping into an easy chair. Mrs. H. remarked, "Could there have been anything in those pills, I feel so very strangely?" Her maid then placed her upon a lounge, and noticed that her hands were tremulous and her eyes closed; but she was quiet, and becoming drowsy. In a few minutes the agitation increased, until it became violent, she, at the same time, kicking out her feet, and throwing her arms forward. She, however, asked for a glass of water. On attempting to move her to her bed, it was found that her limbs were powerless, and that she was unable to stand, so that she had to be carried. It was now observed that her face was "very much flushed, as if she had been standing over the kitchen fire." In a few moments a meddlesome and pleasant delirium set in, in which she picked at her clothes, tried to get out of bed, and imagined she was sewing, or nursing her child, or engaged in shopping with her sister. These hallucinations lasted for about ten minutes, when she sighed and yawned repeatedly, and "dropped into a comfortable sleep," in which state she remained until the arrival of Dr. De Young, at about 10 o'clock; the interval between the taking of the medicine and the sopor having been rather more than one hour.

Dr. De Young found his sister in a lethargic state, from which she could not be aroused. Her face was flushed; her respiration appeared quiet and natural; and there were, now and then, convulsive movements of the hands and feet. An ordinary purgative injection was at once administered, followed, soon afterwards, by an emetic of mustard and warm water. A messenger was sent to the druggist for a copy of the prescription, and, upon his return, it was found that atropia had been substituted for the assafœtida. Dr. De Young then ordered more mustard, along with syrup

of ipecacuanha, which happened to be in the house, and hurried to the drug store to inspect his original prescription. He returned at once, calling for aid on several physicians on his way back, and administered large quantities of emetics, including about five ounces of syrup of ipecacuanha, two ounces of mustard, and one drachm of sulphate of zinc. The enema had produced the desired effect during his absence, but emesis was not excited, although efforts were made in this direction on the part of the patient. The further administration of drugs by the mouth was prevented by the occurrence of trismus.

11.15 A. M. Dr. Charles Carter, of the Northern Dispensary, arrived. The condition of the patient at this time, about three hours after the poison had been taken, is best shown by an extract from his written statement to me: "I found Mrs. H. unconscious, and labouring under a heavy stupor. The eyes were closed, the pupils dilated, and the muscular system was greatly relaxed, excepting a condition of trismus, which was so well-marked that an emetic was administered with great difficulty, and deglutition was almost impossible. The respiration was laboured, and very much like that of an intoxicated person. The pulse was quite good, but neither this nor the respiration was counted." After the lapse of a few minutes Dr. Lewis came in, and, at the suggestion of Dr. Carter, administered a hypodermic injection of half a grain of acetate of morphia.

11.40 A. M. I arrived in company with Dr. Ralph Townsend and Dr. T. H. Andrews, and found Mrs. H. lying perfectly passive in bed, in a state of profound stupor. The muscular system was thoroughly relaxed, the trismus having passed off. The skin was cool and moist; the pulse was 106, of good volume, and pretty strong. The respiration was 26, and heavy, but without stertor. The countenance was somewhat livid. The lids were closed; the conjunctivæ were slightly injected; the pupils were dilated three-fourths and insensible to light; and the eyes had a fixed and brilliant stare. The tongue, roof of the mouth, and soft palate were glazed and parched. Deglutition was impossible, and attempts to introduce remedies by the mouth were attended with suffocative symptoms. I at once threw under the skin half a grain of sulphate of morphia, and washed out the stomach thoroughly, injecting afterwards whiskey and ammonia largely diluted. The effects of the exhibition of the morphia appeared to be scarcely perceptible contraction of the pupil; reduction of the respiration to 20; the production of slight stertor; no change in the pulse. After the use of the stomach-pump, respiration became very irregular and feeble, and, at times, appeared almost to cease. The pupils regained their unnatural size. Faradaism and artificial respiration were now resorted to, the poles of the battery being applied respectively along the course of the phrenic and pneumogastric nerves, and at the hypogastrium. A third half-grain of morphia was again injected at 12 M. Under these measures, after the lapse of fifteen minutes, the respiration was 14, but very decidedly stertorous; and the pulse was 102, pretty full, but weak. The bad condition of the breathing, indicating as it did increased narcotism, was, in my opinion, a sufficient reason for withholding morphia, and from this time no more was exhibited. The stertor continued for half an hour after the induction of artificial respiration.

2 P. M. Professor Gross now arrived, and suggested flagellation of the trunk and extremities with bundles of willow switches, in addition to the other measures employed. In the interval, artificial respiration and faradaism had been unceasingly kept up, the former having been very mate-

rially assisted by slapping the chest and face repeatedly with the hands immersed in ice-water. The mouth was held open by corks, armed with threads to prevent accident, placed between the teeth, and the Marshall Hall method was used. The respiration, at times, was very laboured, and the countenance livid; and whenever the artificial measures were relaxed for a few moments, the breathing threatened to cease entirely, the tongue showing a disposition to fall back and choke up the superior aperture of the larynx, whence it had to be dislodged by the fingers.

6.30 P. M. Up to the present time there has been no change in the symptoms; but now the respiration is 20 and becoming more natural, and permits of short intervals of rest to myself and fatigued assistants. I drew off fourteen ounces of urine, of which I injected twenty drops into the nape of the neck of the family cat, with the effect of widely dilating its pupils. The bowels were found to have acted, and the extremities being cold were enveloped in hot blankets.

7.45 P. M. Artificial respiration, faradaism, and flagellation stopped. Respiration 18. Pulse 108, weak, and of pretty good volume. Muscular system still greatly relaxed. Pupils unchanged. The patient appears to be in a quiet sleep. Two ounces of whiskey were thrown into the rectum, and small lumps of ice were placed in the mouth, the tongue looking like a piece of sole-leather.

8.45 P. M. Respiration began to increase in frequency until it soon reached 30. Inspiration roughened and expiratory murmur much prolonged. Coarse mucous râles abundant throughout the chest. Veins of the face turgid with blood, and death by apnœa imminent, from exhaustion and accumulation of fluid in the air-passages. The former measures were again vigorously resorted to, and, at the suggestion of Professor Gross, veratria ointment, one drachm to the ounce, was briskly rubbed along the spine and over the chest and epigastrium.

9 P. M. Pulse 128; respiration 28. The muscles respond to a weak galvanic current, and the patient opens her eyes, and makes voluntary and quite strong movements, such as drawing up the lower limbs, rolling her head, and twisting the body violently, in response to the flagellation and veratria frictions.

10 P. M. The patient shows signs of returning consciousness. She exclaimed "O my," and turned voluntarily upon her side. At the expiration of ten minutes she attempted to expectorate, and, on being asked if she would take whiskey, nodded affirmatively, and swallowed four tablespoonfuls of equal parts of that fluid and water. The veratria ointment was now discontinued, and Chapman's ice-bag was placed along the spine.

11 P. M. Artificial respiration has been kept up at intervals, and the ice-bag was used about twenty minutes. On being asked how she felt, she replied "Better," and on being slapped, she said, "You hurt me." She now swallowed one tablespoonful of strong beef extract, and a few moments later, she took another with difficulty.

11.10 P. M. Symptoms of suffocation suddenly set in, and notwithstanding an immediate and vigorous resort to the former measures, continued briskly for nearly half an hour, resuscitation was impossible. Death occurred about fifteen hours after taking the poison.

Autopsy, made for the Coroner by Dr. Shapleigh, in the presence of Professor Gross, Dr. Townsend, Dr. De Young, and myself, thirty-eight hours after death, and twenty-four hours after a strong solution of carbolic acid had been thrown into the abdominal cavity.

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Body large and well developed. Some dirty fluid issuing from the mouth and the nose. Rigor mortis well pronounced, and nails purple. Face livid, but not tumid. Pupils dilated one-half; corneæ clear; conjunctivæ not injected, and lids natural. Large suggillations over the back, and the buttocks and posterior surface of the lower limbs livid. The muscles and fasciæ of the dorsal and lumbar regions infiltrated with dark, fluid blood. On opening the spinal column, the dura mater and pia mater were seen to be injected and ecchymosed, while the cord itself was decidedly softened. The vessels of the scalp were distended with liquid blood. The dura mater was wonderfully adherent to the inner surface of the cranium. The vessels of the pia mater were turgid with blood, and there was large subarachnoid serous effusion. The brain tissue was greatly softened, so much so, indeed, that the corpus callosum was torn asunder merely by separating with the fingers the cerebral hemispheres. The lungs were congested and the bronchi filled with mucus. The heart was very soft, readily permitting the finger to be thrust through its walls, and its cavities contained fluid blood. The lining membrane of the aorta and larger vessels was deeply stained, and nowhere in the vascular system was clotted blood found. The intestines were pale, but the stomach presented suggillations at its cardiac extremity. The kidneys were congested. The bladder was empty, and there was no appearance of menstruation.

Remarks.—The dose of atropia, for internal use, at the commencement of the exhibition, is, according to the United States Dispensatory, about one-thirtieth of a grain. In the case now recorded, three grains of the alkaloid were taken, which is a much larger quantity than I find to have been heretofore reported. Some idea of the enormous amount taken may be formed, when I state that that quantity is said by Geiger[1] to be equal to six hundred grains of the extract of belladonna, and by Pfitzner[2] to be the equivalent of seven hundred and twenty grains of the same preparation. The present case, therefore, ought to afford several points of interest, to which I shall briefly invite attention.

The physiological action of atropia on man has of late years been the subject of careful experiment and research, the more recent and most able writers on the topic being Dr. John Harley,[3] and Dr. Meuriot.[4] They both agree that it is a powerful cardiac stimulant in medicinal doses, the force and frequency of the whole circulation, as well as the tone and volume of the arteries, being increased by it. In excessive or poisonous doses, on the other hand, the drug diminishes the force of the heart's action and the tone and volume of the bloodvessels, with only a moderate acceleration of the circulation, or ultimate decrease of the rapidity of the heart's action.

My observations in the case under consideration lead me to coincide in the above statements, with the exception of that which relates to the effect

[1] Professor S. R. Percy. Prize Essay on Atropia. Reprint from the New York Medical Journal, December, 1868.

[2] Ibid.

[3] The Old Vegetable Neurotics. London, 1869.

[4] De la Méthode Physiologique à l'Étude de la Belladone. Paris, 1868.

of excessive doses on the frequency of the circulation. When I first saw the patient, the pulse was 106, at which it remained for eight hours, when it increased two beats. One hour and a quarter later it was 128, which was the maximum reached. The effect of an excessive dose of the drug upon the vascular system may, therefore, be thus expressed: Marked and persistent increase in the rapidity of the circulation; decrease in the force of the pulsations; and loss of volume and tone of the blood-vessels.

Atropia in medicinal doses is generally considered to accelerate the respiration, an opinion particularly insisted upon by Dr. Meuriot. Dr. Harley, however, concludes, from extended observation, that small doses exert no influence whatever upon this function. The inquiries of Dr. Harley refer solely to the action of medicinal doses, and so far these observers agree. But Dr. Meuriot states that the alkaloid in poisonous doses decreases the frequency of the respiratory movements, through paralysis of the pneumogastric nerves. His positive conclusions are not, however, borne out by the experience in the present case, in which the respiration was very decidedly increased in frequency. Thus, at the time of my visit, it was 26, and it was only after eight hours of active treatment that it fell to 18. The subsequent acceleration was doubtless due to exhaustion.

With regard to the cerebro-spinal nervous system, it is usually taught that atropia always produces restlessness, insomnia, and delirium, and that poisonous doses prolong these effects for many hours, until the patient generally passes into coma. Both Dr. Harley and Dr. Meuriot insist upon these effects; but in the case here recorded the restlessness and delirium were evanescent, and, instead of insomnia, lethargy soon set in, and was quickly followed by profound stupor.

The action of the drug on the hollow viscera in this case was somewhat obscure. About two hours after taking the pills, the bowels moved under the stimulus of an injection, and eight hours later, when the patient's urine was drawn off, it was observed that they had acted again. How far this effect was due to the purgative action of the calomel and rhubarb, taken early in the morning, I am unable to decide; nor is it in my power to state whether the urine was passed at the same time. Poisonous doses of belladonna are said to provoke frequent micturition; but this could scarcely have been possible in this case, as I drew off fourteen ounces of urine ten hours after the taking of the drug, and none was found in the bladder after death. Retention of urine had possibly occurred, along with suppression of the secretion from congestion of the kidneys; and this view will appear the more probable when it is remembered that the effects of atropia are much more decided when the quantity of urine is small; in other words, that they are proportionate to the activity of the kidneys, through which organs the alkaloid is principally, if not entirely, eliminated.

Atropia is said to be an emmenagogue. However this may be, no such action could be discovered in the present instance, notwithstanding the fact that the patient had menstruated twenty-seven days previously.

The treatment of poisoning by belladonna and atropia has, of late years, been invested with great interest, particularly with regard to the employment of opium and morphia as antidotes, the mass of evidence being in favour of the view that these agents are mutually antagonistic in their action. So fully impressed was I with this fact, that I took with me, on my visit, sulphate of morphia and a hypodermic syringe, and resorted to the so-called antidote, with the following results.

Nearly three hours after symptoms of poisoning had set in, one-half a grain of acetate of morphia was thrown under the skin. The apparent effect of this was to relieve the trismus. In fifteen minutes half a grain of sulphate of morphia was introduced. This brought down the respiration from 26 to 20, *but produced slight stertor*, and effected no change in the pulse. After the lapse of an additional fifteen minutes, the respiration in the meanwhile having been very irregular and feeble, another half grain was used. In fifteen minutes the pulse was reduced two beats; the respiration was 14, and *very decidedly stertorous;* and the bad breathing continued for half an hour after the vigorous use of artificial respiration and faradaism. A grain and a half of morphia, therefore, used hypodermically during the space of half an hour, merely intensified the poisonous effects of the atropia and still further jeoparded life.

It is not my object to vaunt, or detract from the merits of any particular remedy or treatment, but to furnish facts as they actually occurred, with the view of throwing additional light on a very important and a much-vexed question. With this end in view, I must confess that the experience in this case goes to justify and corroborate the conclusions of Dr. Harley on the question of the antagonistic action of opium and belladonna and their alkaloids. From a careful analysis of the recorded cases, he shows "that the evidence of antagonism in any given case is inconclusive" (p. 309); and "that all the effects of atropia, excepting, perhaps, the influence on the heart, are intensified and prolonged by the action of morphia, induced previously, or at any time during the operation of the former" (p. 291). I may, therefore, be allowed to express the opinion that, in the present state of our knowledge on this subject, it would be unsafe to rely on opium or morphia, to the exclusion of other measures, when an excessive dose of belladonna or atropia has been taken, and particularly so when the system is fully under the effects of the drug.

The good results of artificial respiration were manifest in this case. On several occasions death by apnœa was imminent, when efforts in this direction were relaxed, and to it principally, if not entirely, do I ascribe the remarkable prolongation of life. Hence, I fully indorse the opinion expressed by Dr. Harley that our efforts must be directed to sustain the

breathing in the treatment of poisoning by belladonna. Veratria was also, probably, of essential service. At all events, it proved to be a powerful spinal stimulant.

Professor Percy suggests that, when a large dose of atropia has been taken, and it has become absorbed into the system, much good may be expected from the free administration of diluents. From numerous experiments upon dogs, he concludes—

"As a rule, if atropia is given without water, the effects are much more irritative, and last much longer, than when a sufficiency of water is allowed. When death takes place where water is not allowed, there is always congestion of the kidneys. Morphia, although an antidote to atropia in ordinary cases where water is freely allowed, is hardly an antidote where fluid is entirely withheld. A much larger dose of atropia may be borne without danger, if care is taken to keep the system well supplied with fluids; and the effects of poisoning pass off much more rapidly if warm diluents are prudently administered. Where diluents are freely given, the kidneys perform their function, and gradually remove the poison from the system; but where large doses of the medicine are given unaccompanied with liquids, the kidneys are unable to eliminate either the poison or the urea, and the animal consequently dies, frequently only from uræmic poisoning, at other times from the double effect of the poisoning from the alkaloid, and uræmic poisoning as well." (p. 12.)

When it is remembered that atropia is eliminated principally by the kidneys—elimination by the skin and mucous surfaces being very slight—the foregoing suggestions of Professor Percy would appear to be of value, and should be thoroughly tested.

The post-mortem appearances were of a negative character, as they merely pointed to rapid decomposition. A microscopic examination of the blood, made by myself, disclosed a few shrivelled and crenated corpuscles floating amid others of natural size and shape. Dr. Keen was unable to discover any in the specimen sent to him; but found bodies, which may have been deformed blood-cells, and a large amount of granular matter. The blood never coagulated; it was thoroughly decomposed.

A word in regard to the means of detecting the alkaloid in instances of poisoning by it. The perusal of the case shows that a cat was subjected to the usual physiological test, the injection of the urine of the patient under the skin, the effect of which was dilatation of the pupils. At the post-mortem examination of the body of the deceased, I was enabled to collect about a drachm and a half of the cerebro-spinal fluid, mixed with a little blood, which was afterwards separated from it. On the evening of the 13th of November, or ten days after death, I threw twenty drops of that fluid beneath the skin of the nape of the neck of a kitten. In two minutes the pupils were dilated so widely as to leave the merest line of the irides perceptible. After an hour they were in the same condition; and the kitten had lost its playfulness, avoided the light, and, when it was made to walk, it moved very slowly, as if with hesitation. This experi-

ment, showing as it did how deeply the fluids of the body were saturated with the poison, is entirely novel, and may prove not only of interest to the physiologist, but highly important in a medico-legal point of view.

This case was the subject of criminal action against the druggist who compounded the prescription, at the April term, 1869, of the Oyer and Terminer Court of the First Judicial District of Philadelphia, Judges Brewster and Ludlow presiding. The jury returned a verdict of involuntary manslaughter, with a recommendation to mercy. The counsel for the accused moved, however, for a new trial, and the case is, therefore, undetermined.

In conclusion, I must express my thanks to Professor Gross, Dr. Carter, Dr. Townsend, and Dr. Andrews for their valuable assistance and the unwearied interest which they evinced in the management of the case now recorded.

PHILADELPHIA, July, 1869.